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Detection thresholds of capsaicin: A new test to assess facial skin neurosensitivity

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Synopsis

The goal of this study was to assess the accuracy/reliability of a new test designed to measure cutaneous neurosensitivity. The test was carried out on a random population of 150 healthy adult women and was based on the determination of individual detection thresholds of topically applied capsaicin. Five capsaicin concentrations were used in 10% ethanol aqueous solution (3.16×10^{-5}%; 1×10^{-4}%; 3.16×10^{-4}%; 1×10^{-3}%; 3.16×10^{-3}%). The methodology used to attain the detection threshold was capsaicin application in increasing concentration on the nasolabial folds. The vehicle was simultaneously applied following a split face, single-blind plan. The test was stopped as soon as the subject reported a specific sensation lasting more than 30 seconds on the capsaicin side. The safety of the test was judged as excellent by the panelists since all the reported sensations were considered as slightly or moderately perceptible. The test allowed the classification of the test population according to six threshold levels corresponding to the sensitive reaction to one of the five capsaicin concentrations and to the absence of sensitivity to the highest concentration. Surprisingly, the distribution of the population was not unimodal and seemed to reveal the existence of two different sub-groups: individuals with a low capsaicin detection threshold and those with a high threshold. These two sub-populations strongly differed in their respective self-perception of sensitive skin. The higher the self-declared sensitive skin incidence was, the lower the detection threshold was. This new test of skin neurosensitivity is easy, quick, and truly painless. It appears to be a promising tool for the cosmetic diagnosis of sensitive skin.

INTRODUCTION

Some individuals have a skin that reacts more easily than that of others to certain environmental factors (wind, cold, fast changes in temperature) or to certain topically applied products. This skin reactivity expresses itself, especially on the face, in a variety of discomfort signs (stinging, burning, itching, tingling) associated or not with erythema and scaling (1). This phenomenon is called "sensitive skin." The unpleasant sensations are at least partly due to the stimulation of cutaneous nerve endings specialized in pain transmission, called nociceptors. Different epidemiological surveys have shown that sensitive skin is a common and widespread phenomenon that concerns about 50% of the adult female population in industrialized countries (2–4). There are a lot of similarities

in the perception of sensitive skin by women from different geographical areas (4) and ethnic origins (3). Incidence of self-perceived sensitive skin is lower in the male population (30%) (2,4). It tends to decrease with age (4) and in summer (5). Although these unpleasant cutaneous signs tend to disappear quickly, this condition can render the use of certain kinds of cosmetic product very problematic (2,3). The uncomfortable sensations with no visible signs represent 50% of the reported adverse reactions to cosmetics and toiletries (6) and could be the very first symptoms of an irritant contact dermatitis (7). Consequently, because of the awareness of that problem, cosmetic manufacturers have tried to develop formulations without ingredients likely to induce uncomfortable sensations or containing soothing ingredients intended to decrease skin over-reactivity (8). Products labeled for sensitive skins have met with a growing success: they are purchased by 80% of self-assessed sensitive skin subjects and by 25% of those with non-sensitive skin (9).

Sensitive skin is not a pathological disorder (1). This condition is not easy to assess because it lacks both a consensual definition (9) and visible, physical, or histologically measurable signs. Consequently, there is neither a simple nor pertinent method available to assess sensitive skin (10), unlike the dry or greasy character of skin. The absence of any measurable physical features of self-declared sensitive skin by classic methods has even led some authors to question the reality of this skin condition (11).

Owing to the difficulty in exploring this subjective disorder, psychophysical tests based on the report of sensations induced by topically applied chemical probes have been proposed to identify individuals with sensitive skin and subsequently to test products for "sensitive skin" in this population. The approach was recently validated by functional magnetic resonance imaging (fMRI). The neurophysiological reality of sensitive skin was illustrated by a specific pattern of brain activation in self-assessed sensitive-skin subjects when a chemical probe was applied to their face (12). Moreover, self-reported unpleasant sensations have been reported as a useful tool for irritancy assessment of detergents and soaps (7). In this study, panelists differentiated products in terms of sensation of dryness several washings before observable differences were detected. Nevertheless, much greater attention was given to the visually observable or instrumentally measurable signs of irritation such as redness and inflammation (13).

The lactic acid stinging test, proposed in 1977 (14), relies on the intensity of stinging sensations induced by a lactic acid solution applied on the nasolabial folds. The subjects who report stinging sensations are called "stingers." Using a slightly modified procedure (1), this test is currently performed by cosmetic manufacturers for the selection of "stingers." This selected population prone to experience neurosensory problems with topical products is asked to test new products to substantiate claims indicating that they are appropriate for sensitive skin. Although very useful for product safety, the lactic acid stinging test does not fully render the complexity of self-assessed sensitive skin, as illustrated by the discrepancy between acid lactic response and self-perception of sensitive skin (5,9,10). In 2000, this difference was taken into account for the recommendation to include "stingers" with a concomitant self-declared sensitive skin as panelists for safety testing (9).

Owing to the great similarity of symptoms induced by topically applied capsaicin to those associated with sensitive skin (15), a new elicitation test using a 0.075% emulsion of a pungent compound extracted from chili peppers was proposed in the 1990s to

identify people with sensitive skin (15). Cutaneous application of capsaicin leads to a short release of neurotransmitters (substance P) from peripheral nerve endings and causes the appearance of uncomfortable sensations such as itching, burning, or stinging associated or not with redness at the application site (13,16,17). These unpleasant reactions are more frequent and more intense in self-declared sensitive-skin subjects (15).

Both the lactic acid and capsaicin tests presented above are based on the reported sensations by the subject in terms of nature and intensity and have thus raised controversies owing to the use of a subjective individual pain scale. However, they have been proved to be linked with self-declared sensitive skin because reported sensations were globally stronger and more frequent in sensitive skin subjects. This link with sensitive skin is stronger with capsaicin than with lactic acid (18). The application of a stimulating agent at a single dose (e.g., 10% lactic acid solution or 0.075% capsaicin emulsion) was shown to induce painful sensations, particularly in subjects with very sensitive skin or in a Chinese population as recently reported for lactic acid (19).

In 1998, another psychophysical test based on the assessment of peripheral sensitivity to thermal stimuli was suggested as a possible diagnosis of sensitive skin (20). This test involved the use of a thermal testing instrument—for example, the thermal sensory analyzer (TSA 2001) manufactured by Medoc (Ramat Yishai, Israel)—to assess the thermal functional components of cutaneous nerve endings. The device, called a thermode, delivered thermal stimuli capable of heating or cooling the skin. However, two recent studies showed that this promising test was of limited value in the diagnosis of sensitive skin. In a first study, the link between the detection threshold to thermal stimuli assessed by TSA and self-perceived sensitive skin was not as strong as that observed with skin reactivity to capsaicin and, to a lesser extent, with the lactic acid stinging test (18). In another study, a significant difference in the mean of cold-pain thresholds was reported between sensitive and non-sensitive self-assessed-skin subjects (21). This difference was too weak to consider this thermal parameter as a predictive indicator of sensitive skin.

The interest in using capsaicin in the assessment of sensory skin irritation has recently been confirmed by other authors (22). In addition, the formulation of capsaicin in hydroalcoholic solution has the advantage of accelerating the action of capsaicin on the face in comparison with the previously used 0.075% capsaicin emulsion (13,18).

In the present study, we used the hydroalcoholic solution of capsaicin to develop a test that combines the specific reactivity of sensitive skin to capsaicin, the simplicity of the lactic acid stinging test, and a method of detection threshold. The major goal of this large random population study was to determine if the new method had subsequent advantages in terms of painlessness and accuracy, i.e., if it would be able to rank the subjects on a large range of capsaicin concentration and provide a robust link with self-assessed sensitive skin without being associated with painful sensation.

MATERIALS AND METHODS

SUBJECTS

A total of 150 healthy women participated in this monocenter study carried out in November 2002. Subjects ranged from 18 to 61 years of age (mean = 35). Most of them

lived in an urban environment (Paris or its inner suburbs). No inclusion criterion concerning skin sensitivity was included. The main exclusion criteria were a suspected or known allergy to capsaicin or to chili pepper, the presence of any dermatological, neurological, or vascular disorder in test areas, and the use of any topical or systemic treatment that could modify test findings (dermocorticoids, anti-inflammatories, medicine with central nervous system effect, . . .). This clinical investigation was conducted according to the Declaration of Helsinki principles. The protocol received ethics approval from the CCPPRB of Kremlin-Bicêtre Hospital (Comité Consultatif de Protection des Personnes en Recherche Biomédicale). All volunteers gave written, informed consent acknowledging the understanding of the aim of the study and the procedures involved. Subjects were also informed that they were free to withdraw from the study at any time.

SENSITIVE SKIN QUESTIONNAIRE

Each subject completed a questionnaire concerning skin sensitivity (Table I). This questionnaire contained 20 items and was designed to provide accurate information about self-declared sensitive skin status (existence, symptomatology, factors of skin reactivity). This questionnaire was derived from those used in previous epidemiological surveys on sensitive skin in the UK (2) and in the USA (3).

Table I
Sensitive Skin Questionnaire

	Yes
Do you regard yourself as having a sensitive facial skin?	65.3%
Do you consider yourself as having a facial skin prone to irritation?	43.3%
Do you consider yourself as having a reactive* facial skin?	58.7%
Do you avoid certain cosmetics that you feel may cause your facial skin to react*?	36.7%
Do you consider that your facial skin reacts* readily to cosmetics or toiletries?	34.3%
Do some cosmetics or toiletry products make your facial skin itch, sting, or burn?	42.0%
Have you ever experienced an adverse reaction on your face to a cosmetic or toiletry product?	32.0%
Does the expression "does not tolerate cold weather or a cold environment" apply to your facial skin?	58.0%
Does the expression "does not tolerate hot weather or a hot environment" apply to your facial skin?	27.3%
Does the expression "does not tolerate fast changes in temperature" (e.g., going into a warm shop from a cold street) apply to your facial skin?	50.7%
Does going out in the wind cause your facial skin to itch, burn, or sting?	55.3%
Does going out in the sun cause your facial skin to itch, burn, or sting?	34.0%
Does your facial skin react* to air pollution?	20.7%
Does your facial skin react* to your monthly cycle?	29.3%
Does your facial skin react* to alcoholic drinks?	20.7%
Does your facial skin react* to spicy food?	14.7%
Does your facial skin react* to emotion and/or stress?	48.0%
Have you ever suffered from eczema or dermatitis?	12.7%
Did you suffer from eczema or dermatitis as a child?	10.0%
Have you ever suffered from asthma or hayfever?	12.7%

Subjects had to respond "yes" or "no." The incidence of positive responses is shown for all items.
* Stinging, burning, or itching sensation associated or not with redness.

TEST STIMULI

Six different solutions were used: five test solutions with different concentrations of capsaicin (C1 = 3.16×10^{-5}%; C2 = 1×10^{-4}%; C3 = 3.16×10^{-4}%; C4 = 1×10^{-3}%; C5 = 3.16×10^{-3}% w/w) and the vehicle as control. The vehicle consisted of a 10% ethanol/90% water (w/w) solution prepared using distilled water and absolute ethanol (99.85%, Merck Eurolab®, Briare le Canal, France). Capsaicin is soluble in ethanol, but not in water. Ethanol in high concentrations can induce skin reactivity by itself (13). Hence, formulation experiments regarding capsaicin's stability in hydroalcoholic solutions were previously conducted at the highest capsaicin concentration (C5 = 3.16×10^{-3}%) in order to use the lowest amount of ethanol in the vehicle. In these conditions, capsaicin was stable at ambient temperature for two months. The 3.16×10^{-3}% capsaicin solution was prepared from pure-grade capsaicin powder (8-methyl-*n*-vanillyl-6-nonenamide, ≥98.0%, Fluka®, Buchs, Switzerland). The 3.16×10^{-3}% solution (C5) was diluted using a dilution factor of $\sqrt{10}$ (=3.16) in a stepwise procedure in order to obtain the four other test solutions. The solutions were used at ambient temperature. They were applied by an experimenter employing a single-use cotton tipped applicator (Société Industrielle du Bois®, Saint-Sauveur, France) plunged in the solution, and then rubbed twice on the nasolabial folds. The tubes containing the solutions were customized to control the applied volume and for safety reasons to avoid projections of excess capsaicin solution to the ocular areas. For that purpose, an absorbent sponge was attached to the inside of the tube's neck. Thus, every time the cotton-tipped applicator was removed from the tube, the sponge soaked up any excess solution. In this way, the volume impregnating the applicator was, to a certain extent, standardized. Weighing impregnated applicators before and after application to the face showed that average applied volume was 0.02 ml (+/- 10%).

TEST APPLICATIONS

The major steps of the testing procedure are illustrated in Figure 1. First, the test areas (nasolabial folds) were cleansed using facial cleansing wipes provided by the sponsor. The wipes were impregnated with the vehicle solution and used five times over both test areas. Subjects were excluded from the study if they reported any sensation of discomfort at this stage of the test. Simultaneous split-face application of the vehicle solution over the nasolabial folds followed three minutes after cleansing. The aim of this first step was to familiarize the subject with the humid, cool, and wiping sensations induced by the application and to exclude subjects who felt any discomfort sensation at this step. If no discomfort sensation was reported, the test could continue. Three minutes after the first step, the experimenter performed a single-blind simultaneous split-face application of the vehicle and of the more diluted capsaicin solution (C1 = 3.16×10^{-5}%) over the nasolabial folds. The sides of application of the capsaicin and control solutions were randomized. Subjects were asked to report, during the three minutes following the application, any new sensation or any difference between the test areas, stating precisely the side, the nature (stinging, burning, tingling, itching, other) and the intensity using the following scale: 1 = doubtful, barely perceptible; 2 = slightly perceptible; 3 = moderately perceptible; 4 = strongly perceptible; 5 = painful. The experimenter stopped the test at this point if the reported sensation concerned the capsaicin side and lasted more than 30 seconds. In the absence of any sensation or in the case of any sensation

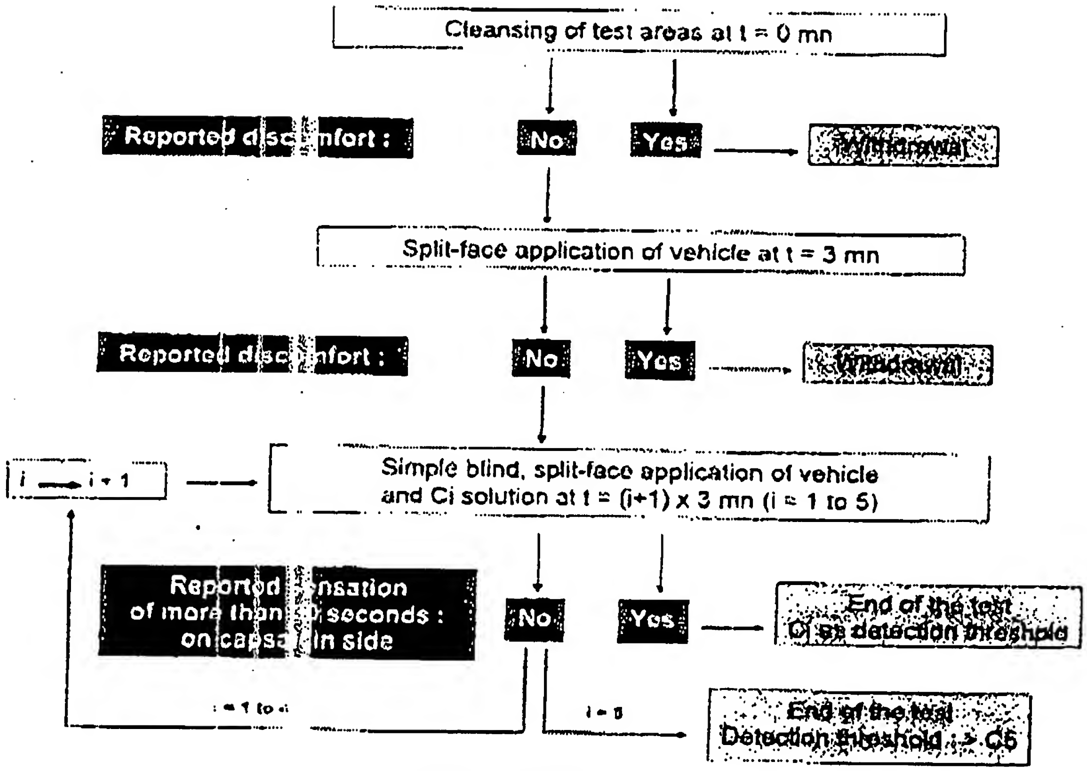

Figure 1. Test diagram.

(irrespective of its intensity or duration) on the vehicle side or any sensation of less than 30 seconds on the capsaicin side, the experimenter continued the test, using the next dose of capsaicin solution and so on, in the increasing order of capsaicin concentration, until the capsaicin side was detected by the subject. A three-minute delay was respected between each stage. The test was stopped as soon as the subject reported a sensation lasting more than 30 seconds on the side of capsaicin application. The last tested concentration was considered as the detection threshold for the subject. Five groups were thus defined based on the threshold (i.e., group C1 = 3.16×10^{-5}%; C2 = 1×10^{-4}%; C3 = 3.16×10^{-4}%; C4 = 1×10^{-3}%; C5 = 3.16×10^{-3}%). If no reaction was reported at the highest concentration, the subject was considered a "non responder" (group "none"). The total duration of the test ranged from nine minutes (C1 solution detected) to 21 minutes (C5 solution applied).

SELECTION OF CAPSAICIN CONCENTRATION

The highest and the lowest concentrated capsaicin solutions, as the dilution factor, were chosen according to the findings of two pilot studies. In a first study on 21 healthy volunteers, we noted that all the test population detected a capsaicin solution below or equal to 1×10^{-2}%. Using a dilution factor of 3.16, we also observed that when a solution was detected, it was always without pain if the previous one had not been detected. But the lowest capsaicin concentration (3.16×10^{-5}%) was still too high and

caused too-significant sensations on two subjects with self-declared very sensitive skin. Thus, a second study was carried out on 11 of the 21 subjects with two more diluted solutions (3.16×10^{-5}% and 1×10^{-4}%). In the latter case, the test was painless, even for the two aforementioned subjects with very sensitive skin. Moreover, the second study allowed us to assess repeatability. On the 11 test subjects, detection thresholds never differed more than one level between two test sessions carried out at a two-week interval.

STATISTICAL METHODS

First, descriptive statistics and graphics were carried out. Percentages of positive response for all items of the questionnaire were tabulated. The distribution of detected capsaicin concentration was described using simple bar charts, as the frequency of self-declared sensitive skin and the mean age of subpopulations ranked by detected capsaicin concentration. Then, different inferential statistics were calculated depending on the nature of the data. For each item of the questionnaire, the association with the detected capsaicin concentration was tested using Kendall's τ_b statistic. The relationship between self-declared sensitive skin and the detection threshold was tested using the Cochran-Armitage trend test. In addition, the influence of age on detected capsaicin concentration was tested using the non-parametric Jonckheere-Terpstra trend test. All results are reported with two-sided p-values. The significance level α was set to 5%. Statistical analysis was carried out using SPSS software (Version 11.00; SPSS Inc., Chicago, IL).

RESULTS

DETECTION THRESHOLDS OF CAPSAICIN

During the initial stages (cleansing or double application of the vehicle), no subjects reported discomfort due to the vehicle, and thus no premature withdrawals occurred before the first capsaicin application. Consequently, the capsaicin detection threshold was determined in the total study population ($n = 150$). Figure 2a shows the distribution of the study population according to capsaicin detection thresholds. Note that the population is distributed among six possible levels: the five capsaicin solutions and the level "none." This distribution shows clearly that there were several different detection thresholds of capsaicin in this general adult female population. As illustrated, the range of detected capsaicin concentration was at least of two log units because 27.3% (N = 41) of the panelists did not reach their detection threshold. More noteworthy about the distribution was its shape. Considering the previous works on sensitive skin typology, one could have expected a unimodal distribution with high frequencies for the mean concentrations and low values for the extreme concentrations. As shown, it was clearly not the case. The pattern of the obtained distribution suggests the existence of at least a bimodal distribution.

RELATIONSHIP WITH SELF-DECLARED SENSITIVE SKIN

The association with detection threshold was established for all the items of the questionnaire. Table II displays Kendall's τ_b values and their significance. Note that the

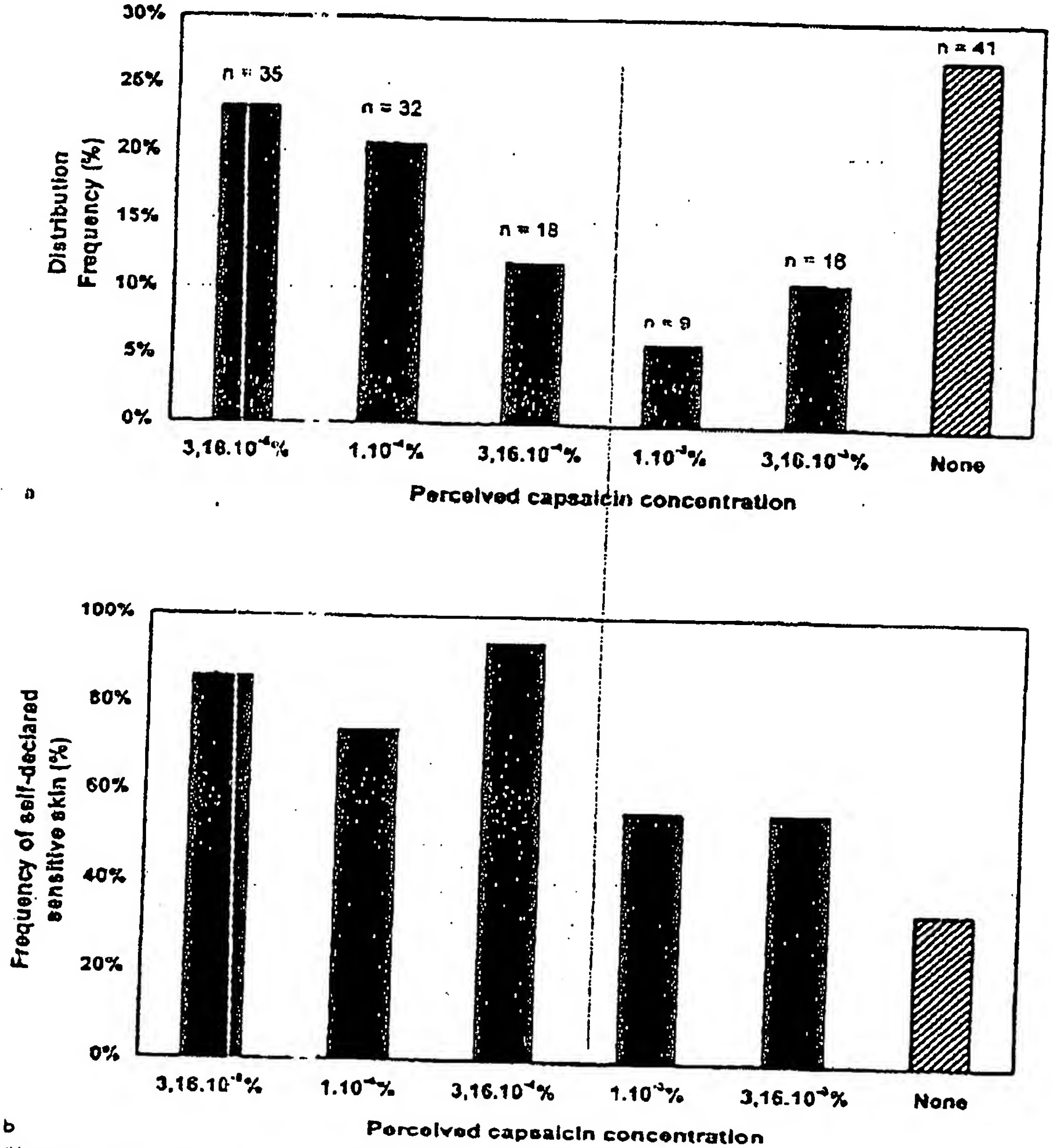

Figure 2. Capsaicin detection thresholds. (a) Distribution of the capsaicin detection thresholds in terms of incidence. (b) Relationship between the capsaicin detection threshold and self-declared sensitive skin. This figure shows the incidence of self-reported sensitive skin in the six subpopulations classified according to detected capsaicin solution.

relationship with the detection threshold was significant for 13 of the 20 items. Interestingly, the most statistically significant link concerned the item "sensitive facial skin" (Kendall's τ_b; $p < 0.001$). Detection thresholds were globally more strongly associated with self-declared skin reactivity to environment (cold, wind, fast changes in temperature) than to cosmetics. The association was highly significant with skin reactivity to

Table II
Links Between Detection Thresholds and Questionnaire Items

	Kendall's τ_b value	p
Do you regard yourself as having a sensitive facial skin?	0.362	<0.001
Does your facial skin react to emotion and/or stress?	0.250	0.001
Does the expression "does not tolerate cold weather or a cold environment" apply to your facial skin?	0.235	0.001
Does going out in the wind cause your facial skin to itch, burn, or sting?	0.229	0.002
Do you consider yourself as having a facial skin prone to irritation?	0.222	0.002
Does the expression "does not tolerate fast changes in temperature" apply to your facial skin?	0.220	0.003
Do you consider yourself as having a reactive facial skin?	0.199	0.006
Have you ever experienced an adverse reaction on your face to a cosmetic or toiletry product?	0.184	0.012
Does the expression "does not tolerate hot weather or a hot environment" apply to your facial skin?	0.182	0.013
Does your facial skin react to your monthly cycle?	0.174	0.017
Does your facial skin react to spicy food?	0.157	0.032
Do some cosmetics or toiletry products make your facial skin itch, sting, or burn?	0.152	0.037
Do you consider that your facial skin reacts readily to cosmetics or toiletries?	0.143	0.050
Did you suffer from eczema or dermatitis as a child?	0.119	0.104
Do you avoid certaian cosmetics that you feel may cause your facial skin to react?	0.115	0.116
Does going out in the sun cause your facial skin to itch, burn, or sting?	0.109	0.138
Does your facial skin react to air pollution?	0.056	0.444
Have you ever suffered from asthma or hayfever?	−0.056	0.447
Does your facial skin react to alcoholic drinks?	0.052	0.476
Have you ever suffered from eczema or dermatitis?	0.032	0.660

Kendall's τ_b values are arranged in decreasing order of statistical significance.

emotion and/or stress and, to a lesser extent, with skin reactivity to spicy food and to the monthly cycle. There was no significant relationship with atopic diathesis and with skin reactivity to air pollution, to alcoholic beverages, or to sun. The strongest association with self-declared facial sensitive skin is illustrated by Figure 2b, which shows its incidence in the six subpopulations classified by the detection threshold. Self-reported sensitive skin incidence was higher than the mean (63.5%) in the three groups who detected the lowest concentrations and lower than the mean for the three others. A very significant trend towards an association between the incidence of self-declared sensitive skin and the capsaicin threshold was noted (Cochran-Armitage; $p < 0.001$). In general, despite a higher incidence found for the concentration 3.16×10^{-4}%, the lower the threshold, the higher the sensitive skin incidence. In addition to the association with the questionnaire items, we studied the correlation with age, known to influence self-perception of sensitive skin. Figure 3 shows the mean age in the six groups. We noted a significant trend toward a relationship between age and detected capsaicin concentration (Jonckheere Terpstra; $p = 0.0142$): the older the subject, the higher the capsaicin detection threshold.

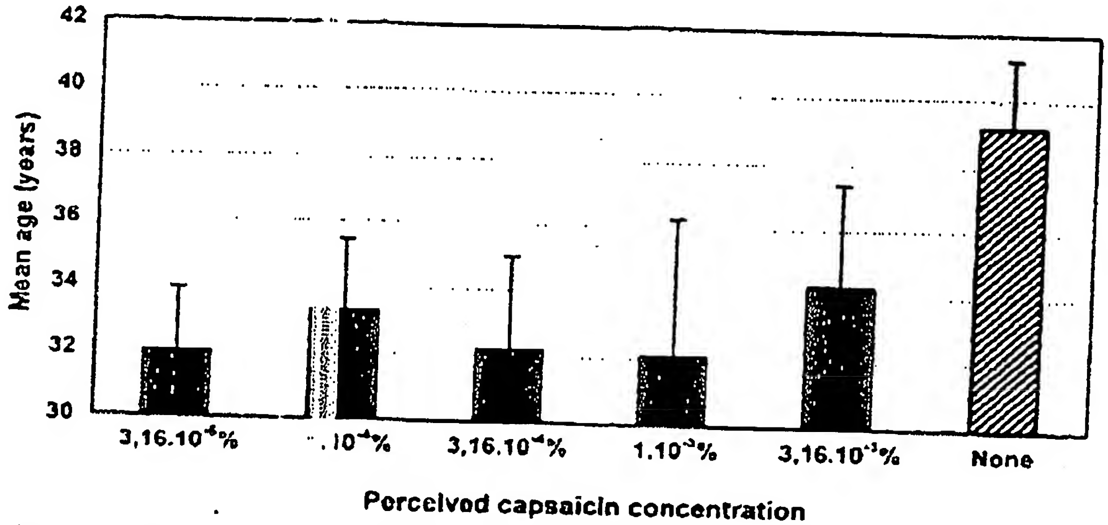

Figure 3. Relationship between the capsaicin detection threshold and age. This figure shows the mean age in the six subpopulations classified according to detected capsaicin solution. Vertical bars denote one standard error of the mean.

REPORTED SENSATION

Table III shows the nature and the intensity of detected sensations in the 109 subjects who reached their detection threshold. A large variety of sensations was reported. The most frequent were stinging and burning sensations, but sensations of tingling, itching, tickling, tightness, coolness, and even a feeling of presence, were also recorded. The great majority of subjects (89.0%) reported only one sensation. The others (11.0%) reported

Table III
Nature and Intensity of the Reported Sensations at Detection Thresholds for the 109 Subjects Who Detected One of the Five Capsaicin Solutions

Nature/Intensity	2	3	M.D.	Total
Stinging sensation	37	4	0	41 (37.6%)
Burning sensation	24	0	1	25 (22.9%)
Tingling sensation	8	1	0	9 (8.3%)
Itching sensation	7	0	0	7 (6.4%)
Feeling of presence	6	0	0	6 (5.5%)
Tickling sensation	5	0	0	5 (4.6%)
Burning and stinging sensations	4	0	1	5 (4.6%)
Stinging sensation and tightness	2	0	0	2 (1.8%)
Stinging and tickling sensations	1	0	0	1 (0.9%)
Stinging and tingling sensations	1	0	0	1 (0.9%)
Itching and tingling sensations	1	0	0	1 (0.9%)
Itching and stinging sensations	1	0	0	1 (0.9%)
Itching sensation and tightness	1	0	0	1 (0.9%)
Burning and tingling sensations	1	0	0	1 (0.9%)
Feeling of coolness	1	0	0	1 (0.9%)
M.D.	2	0	0	2 (1.8%)
Total	102 (93.6%)	5 (4.6%)	2 (1.8%)	109 (100%)

M.D. = missing data.

sensations (e.g., burning and stinging sensations). All the sensations were considered as slightly (intensity 2 = 93.6%) or moderately (intensity 3 = 4.6%) perceptible. They were never reported as strongly perceptible (intensity 4) or painful (intensity 5). In the course of the experiment, the time of onset of sensation at the detection threshold was recorded in 74 of the 109 subjects in order to check that the three-minute interval between applications was long enough. The mean time was 80 seconds +/- 17 s. The shortest time was 60 s and the longest 120 s. On the other hand, a total of 61 subjects reported some sensations before the detection threshold. These sensations appeared on the vehicle side or on the capsaicin side, but they lasted less than 30 seconds in the latter case. These sensations were qualitatively similar to those at the detection threshold described above and concerned the vehicle side as often as the capsaicin side.

DISCUSSION

This study describes a new test for the assessment of skin neurosensitivity on a large cohort. This test consists of applying capsaicin solutions with geometrically increasing concentrations to determine the individual capsaicin detection threshold.

In comparison with the other psychophysical tests using chemical probes (18,19), the test is painless. As expected from topically applied capsaicin (23), a large variety of sensations at the detection threshold were reported. However, all of these sensations were considered as only slightly or moderately perceptible, even in volunteers with the most sensitive skin. The absence of pain is highly advantageous and confirms the right choice of the starting concentration and of the concentration gradient.

This psychophysical test implies a simultaneous, split-face, single-blind application of capsaicin and vehicle solutions. This bilateral procedure, with the simultaneous presentation of the vehicle on the controlateral side as control, helps volunteers to differentiate background cutaneous sensations from those specifically caused by capsaicin (13), and thus avoids false-positive results (24). The single-blinded approach also helps to avoid false-positive results. The test based on the existence of a sensation or not on the capsaicin side is easy to explain to the volunteers and thus far more reliable than those commonly used involving the highly variable individual pain scale.

We observed a large distribution of this random adult female population according to capsaicin detection thresholds (Figure 2a). The lowest capsaicin concentration was detected by 23.3% of the panelists, whereas almost the same proportion (27.3%) did not perceive even the highest concentration, which is one hundred times more concentrated. This range of at least two log units, which looked sizeable, is in agreement with previous results obtained on the arm (23). A more striking feature about the distribution of the population according to the capsaicin detection threshold was its non-unimodal shape. It suggests the existence of (at least) two population groups. Individuals with an intermediate detection threshold account for a low proportion compared to those with either a low or a high detection threshold. Whatever this splitting may mean in terms of "sensitive skin," it appears that, in the tested population, two clearly separated phenotypes are seen with regard to the reactivity to capsaicin through neuron-mediated response. Considering the pattern of Figures 2a and 2b, a segmentation of the population between two sub-populations could be proposed (see vertical line in Figure 2): women

having a detection threshold above or equal to 1×10^{-3}% (44% of the population) could be identified as having a low skin neurosensitivity, and women having a detection threshold below 1×10^{-3}% (56% of the population) could be identified as having a high skin neurosensitivity.

As illustrated in Table I, capsaicin detection thresholds are more strongly linked to self-declared skin reactivity to environment and to emotional stress than to cosmetics. Thus, the capsaicin detection threshold test tends to explore a larger aspect of self-declared sensitive skin than the lactic acid stinging test. To address this question in a more detailed way, further development of the capsaicin detection threshold test shall involve a comparison with the lactic acid stinging test in the same population.

This test should be of particular interest for epidemiological studies designed to assess possible sexual and ethnic variations in skin neurosensitivity. A gender difference observed with this test could be an explanation of the well-documented discrepancy between women and men regarding self-assessed sensitive skin (2,4). It would also enable us to address the question of a possible higher skin neurosensitivity in women, as recently suggested by a study indicating that females show a trend towards being more sensitive to the lactic acid stinging test than males (25). It would also be interesting to explore the reality of the widespread idea that Asian (8) and especially Japanese women (26) would be more prone to subjective symptoms. Significant subjective sensory differences between Japanese and German women have recently been documented using the lactic acid stinging test. Japanese women complained about stronger stinging sensations. In the absence of any measurable differences concerning barrier function and skin reactivity to sodium lauryl sulphate, the authors theorized that this result may reflect a different cultural behavior rather than measurable characteristics in skin physiology (27). Anyway, this possible heightened neurosensitivity in Asian populations does not seem to rely on structural or biochemical particularities of the epidermal fiber network (28). On the contrary, a decrease in epidermal nerve density with age (29) can be evoked to explain the decreased neurosensitivity with age observed in our experiment.

CONCLUSION

This new test of skin neurosensitivity, which is simple, inexpensive, and painless, appears to be a promising prototype for the diagnosis of sensitive skin. Its sensitivity could also provide a basis for the assessment of modulators of skin neurosensitivity. The large distribution of the test population according to capsaicin detection thresholds illustrates the very important interindividual differences concerning the activity of cutaneous nerve endings which are certainly one of the major physiological features explaining the phenomenon of sensitive skin.

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